

Applicant : Yurino, et al.
Serial No. : 09/459,712
Filed : December 13, 1999
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Attorney's Docket No.: 13452-004001 / PH-710US

REMARKS

Status of the Claims

Pending claims

Although Applicants' "after final" response of January 23, 2002, was considered, as noted in paragraph 3 of the Advisory Action mailed March 27, 2002, the proposed amendment was not entered. Thus, claims 7 to 24 are currently pending. Claim 7 has been withdrawn from consideration, thus, claims 8 to 24 are pending and under examination.

Claims canceled and amended

In the instant response, claims 7, 8, 9 and 21 are canceled, without prejudice; and claims 16 and 24 are amended. Thus, after entry of these amendments, claims 10-20 and 22-24 are presented for reconsideration.

Rejections overcome

Applicants thank the Examiner for considering Applicants' "after final" response of January 23, 2002, and, as noted in paragraph 3 of the Advisory Action mailed March 27, 2002, finding that that response overcame the section 112 new matter and second paragraph rejections.

Outstanding Rejections

The rejection under 35 U.S.C. §102(e) that claims 8 to 21, 23 and 24 are allegedly anticipated by U.S. Patent No. 6,023,540 to Walt et al. (hereinafter "Walt") has been maintained, as noted in paragraph 4 of the Advisory Action mailed March 27, 2002.

Applicants respectfully traverse all outstanding objections to the specification and rejections of the claims.

Drawings

Applicants thank the Examiner for approving the drawings.

Issues under 35 U.S.C. §102(e)

The rejection under 35 U.S.C. §102(e) that claims 8 to 21, 23 and 24 are allegedly anticipated by U.S. Patent No. 6,023,540 to Walt et al. (hereinafter "Walt") has been maintained. The Patent Office has maintained the rejections set forth in the previous office action mailed April 9, 2001 to new claims 8 to 24.

In the Advisory Action mailed March 27, 2002, paragraph 4, the Patent Office alleged that the claim wording directed to amount still did not distinguish [the claimed invention] over Walt, et al. (referring to the proposed amendment to claims set forth in Applicants "after final" response of January 23, 2002, which was not entered, although the response was considered). The Patent Office further alleged that that Walt, et al., also determines sample amounts and thus also normalizes, as does the instant invention.

The legal standard for anticipation under 35 U.S.C. §102 is one of strict identity. To anticipate a claim, a single prior source must contain each and every limitation of the claimed invention

Applicants maintain that Walt does not disclose each and every limitation of the claimed invention and, therefore, does not render the claims unpatentable. Walt does not teach or suggest a method for detecting a degree of hybridization between a probe and a sample comprising, *inter alia*, providing a substrate on which each of a plurality of types of probes are separately immobilized on each different and separate position and where the probes are labeled with a first detectable label, detecting an amount of the probe at each position of the substrate by detecting the first detectable label and producing a value representing the degree of hybridization between a probe and a sample by normalizing the difference between the amount of the probe and the amount of the sample nucleic acid hybridized to the probe with the amount of the probe.

The Patent Office has noted that in Walt the quantifying of microspheres with probes on them is deemed a quantifying of probes, albeit not of probe number *per se*.¹

In fact, in the claimed methods the probe number *per se* is detected. This is clarified by the instant amendment; after entry of the amendment the claims will read "detecting

¹ See the last paragraph, particularly the last three lines, of page 4 of the final Office Action mailed 01/23/01.

the amount of the probe at each position of the substrate.” Walt does not disclose detecting the amount of the probe at each position of a substrate.

As noted by the Patent Office, Walt does not measure probe number *per se* on their microspheres; the quantifying of microspheres with probes on them is not a quantifying of the number of probes. The amount of probes on a microsphere can vary greatly from microsphere to microsphere; thus, it does not follow that quantifying of microspheres is a quantifying of probes. For example, in contrast to the teachings of Applicants' invention, probes 60a, 60b, and 60c of Walt are not labeled with fluorescent marker dyes (Fig. 3 of Walt), and, therefore, cannot be measured by any means taught in Walt.

Moreover, there is no suggestion or motivation in Walt to quantify the amount of probes on a microsphere. In fact, Applicants submit that quantifying the amount of probes on a microsphere was not even contemplated in Walt, as it does not relate to the objectives of Walt. Therefore, while Walt may teach the quantifying of microspheres, it does not teach the quantifying of probes. Applicants have amended independent claims 16 and 24 to recite that the claimed method includes detecting the amount of the probe at each position of the substrate. Support for such amendment can be found, *inter alia*, on page 5, lines 30-32 of the instant specification.

The Patent Office has noted that the “argued number of probe molecules is not an instant claim limitation. Rather the instant claims only indicate an ‘amount’ which lacks any numerical requirement that would distinguish the instant claims from the reference which determines an amount via a normalizing signal.”²

Applicants aver that the instant claims do not need to recite a numerical requirement to distinguish them over Walt. In column 15, lines 25-36 of Walt, “normalizing” refers to determining the level of background signal. Applicants do not use “normalizing” to determine the level of background signal. In the instant invention, “normalizing” is used to determine the difference between the amount of the probe biopolymer spotted on the substrate relative to the amount of sample biopolymer. Thus, the claimed invention is distinguishable over Walt without a recitation of a numerical requirement.

² See page 5, lines 3-8 of the final Office Action mailed 01/23/01.

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In light of the amendment to the claims, and reasons provided, Applicants submit that Walt does not disclose each and every limitation of the claimed invention. Accordingly, Applicants aver the rejection to claims under section 102, can be properly withdrawn.

CONCLUSION

In view of the foregoing remarks and amendment, it is believed that the all claims pending in this application (after entry of the instant amendment) are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

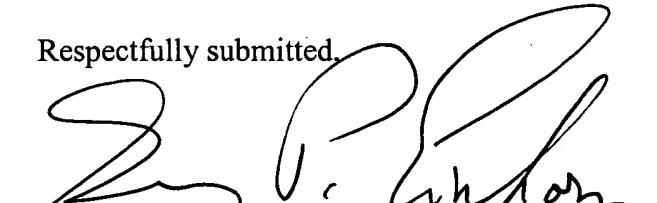
If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at (858) 678-5070.

Applicants believe that no fees are necessitated by the present Response. However, in the event any fees are due, the Commissioner is hereby authorized to charge any such fees to Deposit Account No. 06-1050.

Respectfully submitted,

Date:

May 15, 2002


Gregory P. Einhorn
Reg. No. 38,440

Fish & Richardson P.C.
4350 La Jolla Village Drive, Suite 500
San Diego, California 92122
Telephone: (858) 678-5070
Facsimile: (858) 678-5099



Version with markings to show changes made

Applicant : Yurino, et al.

Art Unit : 1631

Serial No. : 09/459,712

Examiner : Arden Marschel, Ph.D.

Filed : December 13, 1999

Title : HYBRIDIZATION DETECTION METHOD AND BIOCHIPS

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In the claims:

Claims 7, 8, 9 and 21 have been canceled, without prejudice.

The claims have been amended as follows:

16. (Amended) A method for detecting [the] a degree of hybridization [binding] between a probe and a sample comprising a biopolymer, the method comprising

(a) providing a substrate on which each of a plurality of types of probes is separately immobilized on each different and separate position [are immobilized at a given position], wherein the probes are labeled with a first detectable label;

(b) providing a sample comprising a biopolymer, wherein the biopolymer is labeled with a second detectable label;

(c) contacting the sample with the probe; [and]

(d) detecting [the] an amount of the probe at each position of the substrate by detecting the first detectable label; [and]

(e) detecting an [the] amount of the sample biopolymer bound to the probe at each position of the substrate by detecting the second detectable label; and

(f) [(d)] producing a value representing the degree of hybridization [binding] between a probe and a sample biopolymer by normalizing the difference between the amount of the probe and the amount of the sample biopolymer [bound] hybridized to the probe with the amount of the probe.

VERSION WITH MARKINGS TO SHOW CHANGES MADE

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24. (Amended) A method for detecting a [the] degree of hybridization between an oligonucleotide probe immobilized onto an array and a sample nucleic acid, the method comprising

(a) providing a substrate on which each of a plurality of types of oligonucleotide probes is separately immobilized on each different and separate position [are immobilized at a given position] to form an array, wherein the oligonucleotide probes are labeled with a first detectable label;

(b) providing a sample comprising a nucleic acid, wherein the nucleic acid is [acids are] labeled with a second detectable label;

(c) contacting the sample with the probe; [and]

(d) detecting [the] an amount of the probe at each position of the substrate by detecting the first detectable label; [and]

(e) detecting an [the] amount of the sample nucleic acid hybridized to the probe at each position of the substrate by detecting the second detectable label; and

(f) [(d)] producing a value representing the degree of hybridization between a probe and a sample by normalizing the difference between the amount of the probe and the amount of the sample nucleic acid hybridized to the probe with the amount of the probe.